Exhibit CC

Letters | September 2021

Annals of Internal Medicine

Safety and Immunogenicity of Anti–SARS-CoV-2 Messenger RNA Vaccines in Recipients of Solid Organ Transplants

FREE

Olivier Marion, MD, Arnaud Del Bello, MD, Florence Abravanel, PharmD, PhD, ... View all authors +

Author, Article and Disclosure Information

https://doi.org/10.7326/M21-1341

Background: Recipients of solid organ transplant (SOT) are a high-risk group for severe SARS-CoV-2 infection. The mortality rate of patients with SOT during the COVID-19 pandemic has been reported to be approximately 20% (1). The anti–SARS-CoV-2 vaccines represent a hope to protect this population against this life-threatening infection.

Objective: To assess the humoral response to messenger RNA (mRNA)–based vaccination in recipients of SOT.

Methods: All patients with heart, kidney, liver, or pancreas transplants from the Midi-Pyrénées region (southwest France) are followed in our department. When the vaccination campaign started (7 January 2021), these patients were invited via text message, e-mail, or transplant patients' associations to be vaccinated. Patients were asked to register via a dedicated telephone number or website. They were vaccinated consecutively according to their registration date. According to the recommendations of the Francophone Society of

Transplantation, anti–SARS-CoV-2 spike protein antibodies were monitored before and after vaccination. We used the SARS-CoV-2 total antibodies enzyme-linked immunosorbent assay test (Beijing Wantai Biological Pharmacy Enterprise) (80% of patients) or another validated anti–SARS-CoV-2 spike protein assay. According to French law (*loi Jardé*), anonymous retrospective studies do not require institutional review board approval.

Findings: By 16 April 2021, 950 patients of the 2666 from our cohort had received at least 1 dose of an mRNA vaccine (BNT162b2 vaccine [Pfizer-BioNTech], $n = 942$; mRNA-1273 vaccine [Moderna], $n = 8$) and had anti–SARS-CoV-2 antibodies monitored. Fifty patients had vaccination without monitoring of antibodies, 80 patients are planned to be vaccinated within the next month, and 257 patients declined the vaccine. We had no feedback from the remaining 1329 patients.

A total of 895 of the 950 patients had an available serologic screening just before the first injection. The prevalence of anti–SARS-CoV-2 antibodies was 2.1% (95% CI, 1.3% to 3.3%; $n = 19$ of 895). Only 5 of the 19 patients who were seropositive previously had symptomatic COVID-19. A total of 576 patients benefited from a second injection at day 28. The prevalence of anti–SARS-CoV-2 antibodies before the second injection was 6.4% (CI, 4.6% to 8.8%; $n = 37$ of 576).

In 367 patients who had a 4-week follow-up after the second dose, the prevalence of anti–SARS-CoV-2 antibodies increased from 1.4% (CI, 0.4% to 3.2%; $n = 5$ of 367) at baseline to 6.3% (CI, 4.0% to 9.3%; $n = 23$ of 367) at day 28 and 33.8% (CI, 29.0% to 38.9%; $n = 124$ of 367) 1 month after the second dose (Figure). Characteristics of patients who were vaccinated with and without a 4-week follow-up after the second dose are presented in the Table.

Figure. Prevalence of anti–SARS-CoV-2 antibodies at 4 wk after the second vaccine dose in all transplant patients and by type of organ transplant.

Percentages with exact binomial 95% CIs are presented.

Download figure | Download PowerPoint

Table Characteristics of Recipients of SOT With and Without a 4-Week Follow-up After 2-Dose Messenger RNA–Based Vaccination

The tolerance of mRNA vaccines was excellent, with no serious adverse events reported, except in 1 patient with a liver transplant who developed paresthesia of the lower limb. Kidney function and liver enzymes remained stable in recipients of kidney and liver transplants before and 28 days after the first dose (data not shown). One recipient of a kidney transplant presented 3 weeks after the first injection with a 50% increase in serum creatinine level related to drug-induced dehydration. The patient recovered after rehydration and reduction of diuretics. Only 1 patient, who had vaccination without the requested biological monitoring and who is not included in this report, had an acute cellular rejection.

Discussion: In immunocompetent patients, mRNA vaccines have shown strong antibody response, even after a single dose (2). In immunocompromised patients, such as recipients of SOT, a weak humoral response to mRNA vaccines was reported. Boyarsky and colleagues (3) reported the appearance of specific antibodies in 17% of transplant recipients 3 weeks after a single dose of an mRNA vaccine. Recently, in a small series of patients with SOT, including mainly those who had a kidney transplant, anti–SARS-CoV-2 antibodies were detected in 37.5% to 58.8% of patients at 4 weeks after the second dose (4, 5). Our

study, which included many patients with SOT, confirms a weak immunogenicity of mRNA vaccines in those who had a transplant. Recipients of liver transplant showed a better humoral response than recipients of other organs. Considering the good tolerance of mRNA vaccines, an increased antigen dose or a third vaccine dose can be proposed to improve the vaccination response in this specific population. In France, the French National Authority for Health has recently recommended offering a third dose to immunosuppressed patients.

Further studies are required to assess both cellular and humoral responses to vaccines and to determine their long-term protective capacity. Meanwhile, enhanced barrier measures should be maintained, and vaccination of household members and close contacts is recommended.

Comments

0 Comments

SIGN IN TO SUBMIT A COMMENT

PREVIOUS ARTICLE

NEXT ARTICLE